

TABLE 2

Oral Bioavailability in Monkeys					
	Dose (mg)	AUC (ng/mL × h)	Norm AUC (ng/mL × h/mg)	Mean Norm AUC (ng/mL × h/mg)	F (%)
IV Monkey 1	46.44	13614	293.2		
IV Monkey 2	24.53	6581	268.3		
IV Monkey 3	20.72	6079	293.4	284.9	
PO Monkey 1	29.04	758	26.1		
PO Monkey 2	30.93	898	29.0		
PO Monkey 3	30.04	1842	61.3	38.8	13.6

TABLE 3

Experimental Pharmacokinetics of β -D-2'-CH ₃ -riboG in Cynomolgus Monkeys		
	IV	PO
Dose/Route (mg/kg)	10	10
C _{max} (ng/mL)	6945.6 ± 1886.0	217.7 ± 132.1
T _{max} (hr)	0.25 ± 0.00	2.00 ± 1.00
AUC (ng/mL × hr)	8758.0 ± 4212.9	1166.0 ± 589.6
T _{1/2} (hr)	7.9 ± 5.4	10.3 ± 4.1
CL (L/hr/kg)	1.28 ± 0.48	
V _{ss} (L/kg)	2.09 ± 0.54	
F (%)		13.8

Example 6

Bone Marrow Toxicity Assay

Human bone marrow cells were collected from normal healthy volunteers and the mononuclear population was separated by Ficoll-Hypaque gradient centrifugation as described previously by Sommadossi J-P, Carlisle R. "Toxicity of 3'-azido-3'-deoxythymidine and 9-(1,3-dihydroxy-2-propoxymethyl)guanine for normal human hematopoietic progenitor cells in vitro" Antimicrob Agents and Chemotherapy 1987; 31:452-454; and Sommadossi J-P, Schinazi R F, Chu C K, Xie M-Y. "Comparison of cytotoxicity of the (-) and (+)-enantiomer of 2',3'-dideoxy-3'-thiacytidine in normal human bone marrow progenitor cells" Biochemical Pharmacology 1992; 44:1921-1925. The culture assays for CFU-GM and BFU-E were performed using a bilayer soft agar or methylcellulose method. Drugs were diluted in tissue culture medium and filtered. After 14 to 18 days at 37° C. in a humidified atmosphere of 5% CO₂ in air, colonies of greater than 50 cells were counted using an inverted microscope. The results in Table 4 are presented as the percent inhibition of colony formation in the presence of drug compared to solvent control cultures.

TABLE 4

Human Bone Marrow Toxicity CFU-GM and BFU-E Clonogenic Assays		
Treatment	IC ₅₀ in μ M	
	CFU-GM	BFU-E
ribavirin	~5	~1
β -D-2'-CH ₃ -riboA	>100	>100
β -D-2'-CH ₃ -riboU	>100	>100
β -D-2'-CH ₃ -riboC	>10	>10
β -D-2'-CH ₃ -riboG	>10	>100

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Example 7

Mitochondria Toxicity Assay

HepG2 cells were cultured in 12-well plates as described above and exposed to various concentrations of drugs as taught by Pan-Zhou X—R, Cui L, Zhou X-J, Sommadossi J-P, Darley-Usmer V M. "Differential effects of antiretroviral nucleoside analogs on mitochondrial function in HepG2 cells" Antimicrob Agents Chemother 2000; 44:496-503. Lactic acid levels in the culture medium after 4 day drug exposure was measured using a Boehringer lactic acid assay kit. Lactic acid levels were normalized by cell number as measured by hemocytometer count. The preliminary results from this assay are tabulated in Table 5.

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TABLE 5

Mitochondrial Toxicity Study (L-lactic acid assay)			
	Conc. (μ M)	lactate (mg/10 ⁶ cell)	% of Control
Control		2.18	
FIAU	10	3.73	170.4
β -D-2'-CH ₃ -riboC	1	2.52	115.3
	10	2.36	107.9
	50	2.26	103.4
	100	2.21	101.2

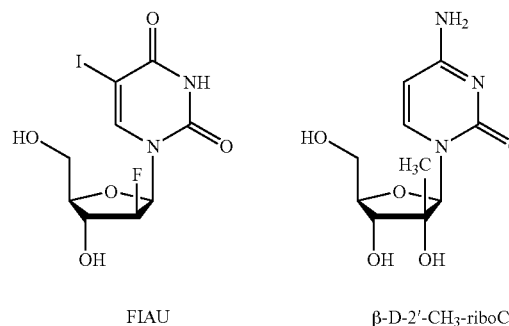
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This invention has been described with reference to its preferred embodiments. Variations and modifications of the invention, will be obvious to those skilled in the art from the foregoing detailed description of the invention.

We claim:

1. A method for the treatment of a hepatitis C virus infection, comprising administering an effective amount of a purine or pyrimidine β -D-2'-methyl-ribofuranosyl nucleoside or a phosphate thereof, or a pharmaceutically acceptable salt or ester thereof.

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